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PRVD2007-10

Proposed Re-evaluation Decision

Metalaxyl and Metalaxyl-M

(publié aussi en français)

5 November 2007

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 978-0-662-47148-6 (978-0-662-47149-3)

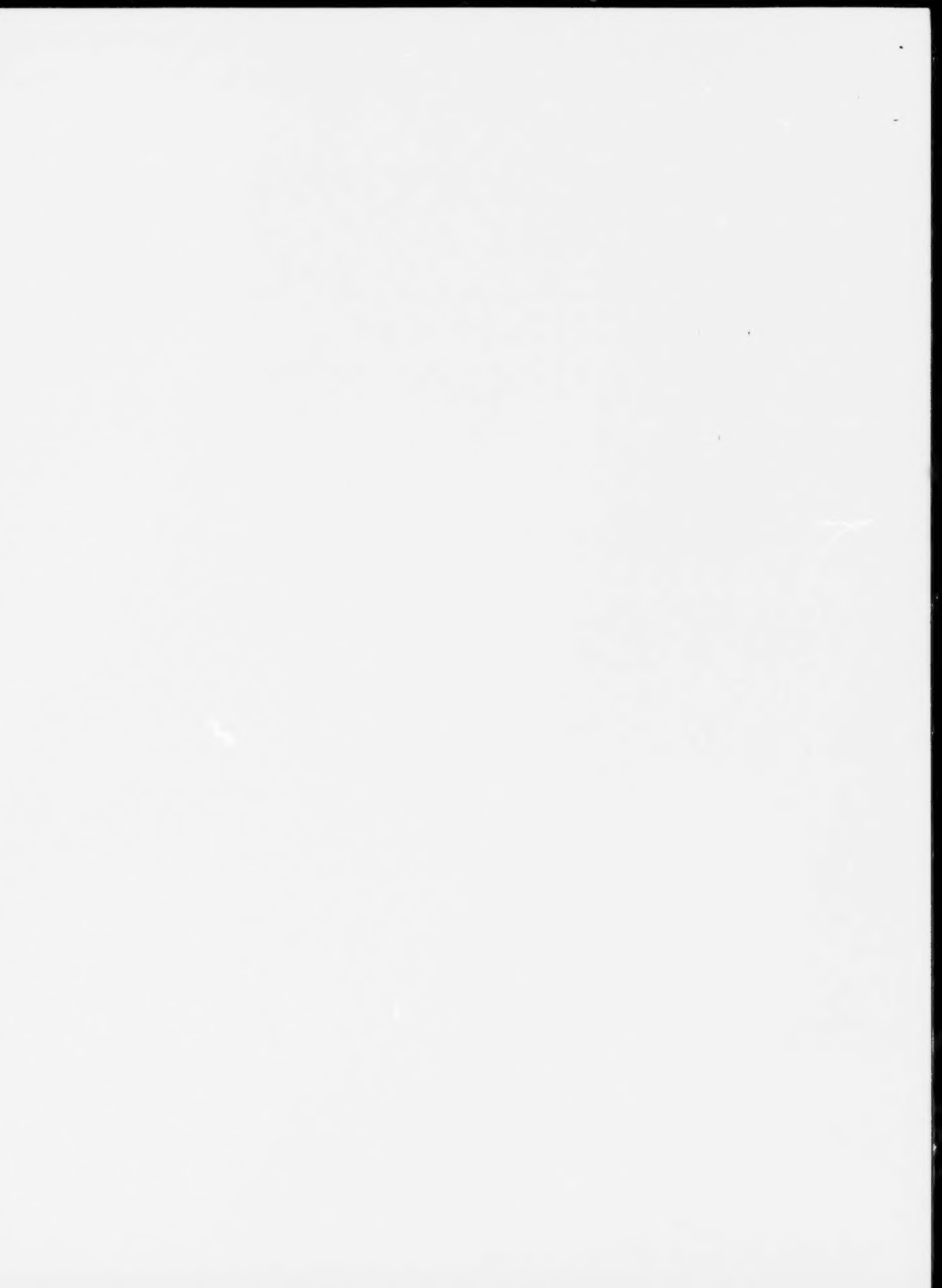
Catalogue number: H113-27/2007-10E (H113-27/2007-10E-PDF)

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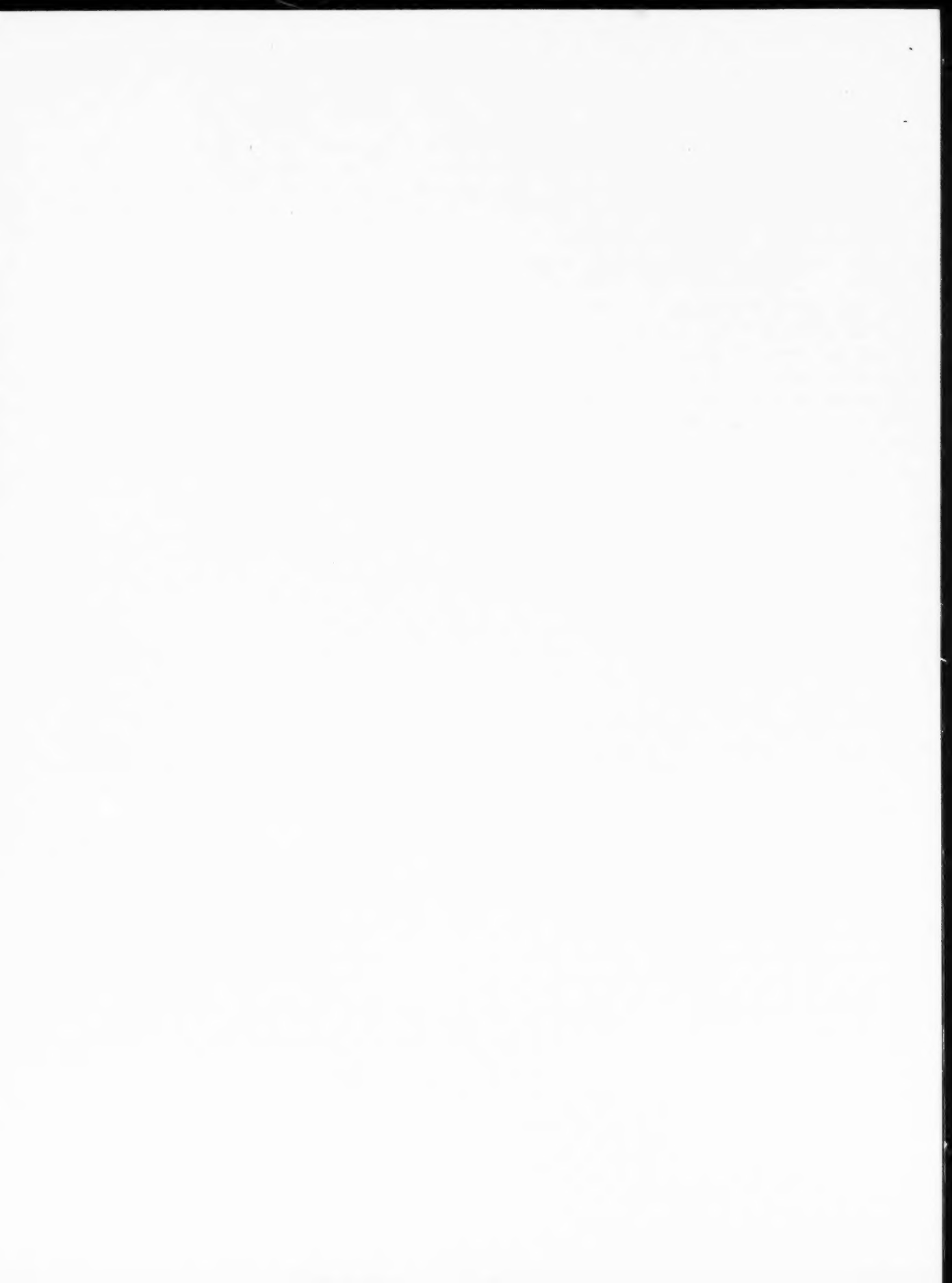
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Table of Contents

Overview	1
What Is the Proposed Re-evaluation Decision?	1
What Does Health Canada Consider When Making a Re-evaluation Decision?	1
What Are Metalaxyl (the racemic mixture) and Metalaxyl-M (the R-enantiomer)?	2
Health Considerations	3
Environmental Considerations	4
Measures to Minimize Risk	5
What Additional Scientific Information Is Required?	5
Next Steps	5
Science Evaluation	6
1.0 Introduction	6
2.0 The Technical Grade Active Ingredient, Its Properties and Uses	6
2.1 Identity of the Technical Grade Active Ingredient	6
2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient	8
2.3 Comparison of Use Patterns in Canada and the United States	8
3.0 Impact on Human Health and the Environment	9
3.1 Human Health	10
3.1.1 Occupational Exposure and Risk Assessment	10
3.1.2 Non-Occupational Exposure and Risk Assessment	12
3.1.3 Cumulative Effects	16
3.2 Environment	16
3.2.1 Environmental Risk Assessment	16
3.2.2 Toxic Substances Management Policy Considerations	18
4.0 OECD Status of Metalaxyl and Metalaxyl-M	19
5.0 Proposed Re-evaluation Decision	20
6.0 Data Required as Condition of Continued Registration	20
7.0 Supporting Documentation	20



List of Abbreviations	23
Appendix I Additional Data Requirements	25
Appendix II Products Containing Metalaxyl and Metalaxyl-M and Registered in Canada as of 4 July 2007	27
Appendix III Toxicological Endpoints Selected by the USEPA for the Metalaxyl and Metalaxyl-M Health Risk Assessments	29
Appendix IV Label Amendments for Products Containing Metalaxyl (racemic mixture) and Metalaxyl-M (R-enantiomer)	31
Appendix V Inputs to Buffer Zone Models for Metalaxyl-M	35



Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the fungicide metalaxyl (the racemic mixture) and metalaxyl-M (the R-enantiomer), Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing racemic mixture and R-enantiomer in Canada.

An evaluation of available scientific information found that products containing racemic mixture and R-enantiomer do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of the racemic mixture and R-enantiomer uses, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

This proposal affects all end-use products containing the racemic mixture and R-enantiomer registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document¹ that summarizes the science evaluation for the racemic mixture and R-enantiomer and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the re-evaluation process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of the racemic mixture and R-enantiomer.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive *DIR2001-03, PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Metalaxyl racemic mixture and R-enantiomer, two of the active ingredients in the current re-evaluation cycle, have been re-evaluated under the Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy).

The PMRA is re-evaluating active ingredients and their uses to determine their continuing acceptability in relation to human health, environment and value. Metalaxyl (the racemic mixture) and metalaxyl-M (the R-enantiomer) are two of the active ingredients to be re-evaluated during the current re-evaluation cycle. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

The USEPA conducted a re-evaluation of the racemic mixture and R-enantiomer, and conclusions of this re-evaluation are published in a 1994 RED. In addition, an aggregate risk assessment was published in 2001 in the Federal Register. On the basis of health and environmental risk assessments, the USEPA concluded that the racemic mixture and R-enantiomer were eligible for reregistration with the implementation of risk-reduction measures. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED and in the 2001 Federal Register were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Are Metalaxyl (the racemic mixture) and Metalaxyl-M (the R-enantiomer)?

The racemic mixture and R-enantiomer are systemic fungicides used to control plant diseases caused by water-mould fungi (*Oomycetae*) in field and greenhouse food and feed crops (including seed treatment) as well as nursery outdoor and greenhouse non-food crops (including conifers, ornamentals and turf).

Health Considerations

Can Approved Uses of the Metalaxyl Racemic Mixture and R-enantiomer Affect Human Health?

Additional risk-reduction measure statements are required on the racemic mixture and R-enantiomer labels. The racemic mixture and R-enantiomer are not likely to affect human health when used according to the revised label directions.

People could be exposed to the racemic mixture and R-enantiomer by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that the racemic mixture and R-enantiomer were unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

The metalaxyl racemic mixture and R-enantiomer are currently registered in Canada for use on seed (alfalfa, barley, bean, beet, canola, chick pea, clover, forage grasses, turf grasses, lentil, oat, pea, rapeseed, rye, sainfoin, sorghum, sunflower, trefoil, vetch and wheat), non-bearing apple, bean, blueberry, carrot, cucumber, ginseng, grape, hop, lettuce, onion, potato, raspberry, strawberry, tobacco, ornamentals, conifers and turf. The racemic mixture and R-enantiomer could be used in other countries on crops that are imported into Canada.

In Canada, MRLs for the racemic mixture have been established for the following commodities:

- green onions and spinach at 10 ppm;
- asparagus at 7 ppm;
- citrus fruits, endives and lettuce at 5 ppm;

- avocados at 4 ppm;
- ginseng and dry onions at 3 ppm;
- blueberry, broccoli, cabbage, cauliflower and raisins at 2 ppm;
- apricot, cantaloupe, cherry, cucumber, grape, peach/nectarine, peppers, plum, soybean, squash, sugar beet molasses, tomato and watermelon at 1 ppm;
- almond, carrot, potato, radish and walnut at 0.5 ppm;
- strawberry at 0.4 ppm;
- beans, peanut, pea, raspberry and wheat at 0.2 ppm; and
- barley at 0.05 ppm.

Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in the Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

Environmental Considerations

What Happens When the Metalaxyl Racemic Mixture and R-enantiomer Are Introduced Into the Environment?

The racemic mixture and R-enantiomer are unlikely to affect non-target organisms when used according to the revised label directions. Additional risk-reduction measures are required on the racemic mixture and R-enantiomer labels.

Non-target organisms (e.g. birds, mammals, insects, aquatic organisms and terrestrial plants) may be exposed to the racemic mixture and R-enantiomer in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the expected environmental concentration to the relevant effects endpoint of concern. The resulting risk quotients are compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a negligible risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some degree of risk.

The USEPA concluded that the reregistrations of the metalaxyl racemic mixture and R-enantiomer were acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of the racemic mixture and R-enantiomer, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- To protect mixer/loader/applicators: additional protective equipment
- To protect workers re-entering treated sites: a restricted-entry interval

Environment

- To reduce potential surface and groundwater contamination: additional advisory label statements

What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter.

Appendix I lists all data requirements.

Next Steps

Before making a final re-evaluation decision on the racemic mixture and R-enantiomer, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision² document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

² "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

Metalaxyl (racemic mixture) and metalaxyl-M (R-enantiomer) are fungicides that act by the inhibition of protein (RNA) synthesis in fungi.

Following the re-evaluation announcement for the racemic mixture and R-enantiomer, the registrants of the technical grade active ingredients in Canada indicated that they intended to provide continued support for all uses included on the labels of commercial and domestic end-use products in Canada.

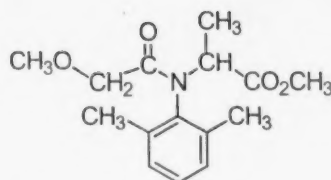
The PMRA used recent assessments of the racemic mixture and R-enantiomer from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for metalaxyl, dated September 1994, and a Federal Register document in 2001 for metalaxyl-M, as well as other information on the regulatory status of the racemic mixture and R-enantiomer in the United States, can be found on the USEPA's website at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

a) Metalaxyl (racemic mixture)

Common name	Metalaxyl
Function	Fungicide
Chemical family	Phenylamide
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	<i>N</i> -(methoxyacetyl)- <i>N</i> -(2,6-xylyl)-DL-alaninate
2 Chemical Abstracts Service (CAS)	<i>N</i> -(2,6-dimethylphenyl)- <i>N</i> -(methoxyacetyl)-alanine methyl ester
CAS Registry Number	57837-19-1
Molecular formula	C ₁₅ H ₂₁ NO ₄

Structural formula**Molecular weight**

279.3 amu

b) Metalaxyl-M (the R-enantiomer)**Common name**

Metalaxyl-M

Function

Fungicide

Chemical family

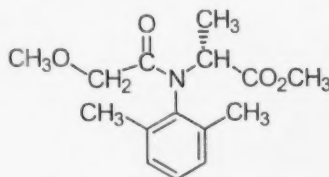
Phenylamide

Chemical name

- | | | |
|---|---|--|
| 1 | International Union of Pure and Applied Chemistry (IUPAC) | Methyl <i>N</i> -(methoxyacetyl)- <i>N</i> -(2,6-xylyl)-D-alaninate |
| 2 | Chemical Abstracts Service (CAS) | Methyl <i>N</i> -(2,6-dimethylphenyl)- <i>N</i> -(methoxyacetyl)-D-alaninate |

CAS Registry Number

70630-17-0

Molecular formula $C_{15}H_{21}NO_4$ **Structural formula****Molecular weight**

279.3 amu

Based on the manufacturing process, metalaxyl and metalaxyl-M are not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy Track-1 substances as identified in Appendix II of Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Metalaxyl (the racemic mixture)

Property	Result
Henry's law constant	$1.6 \times 10^{-5} \text{ Pa m}^3 \text{ mol}^{-1}$ (calculated)
<i>n</i> -Octanol—water partition coefficient	$\log K_{ow} = 1.75$ (25 °C)
Solubility in water	8.4 g/L (22 °C)
Ultraviolet (UV) / visible spectrum	Not expected to absorb UV at $\lambda > 300 \text{ nm}$
Vapour pressure	0.75 mPa (25 °C)

Metalaxyl-M (the R-enantiomer)

Property	Result
Henry's law constant	$3.5 \times 10^{-5} \text{ Pa m}^3 \text{ mol}^{-1}$ (calculated)
<i>n</i> -Octanol—water partition coefficient	$\log K_{ow} = 1.71$ (25 °C)
Solubility in water	26 g/L (25 °C)
Ultraviolet (UV) / visible spectrum	Not expected to absorb UV at $\lambda > 300 \text{ nm}$
Vapour pressure	3.3 mPa (25 °C)

2.3 Comparison of Use Patterns in Canada and the United States

Metalaxyl racemic mixture and R-enantiomer are fungicides registered in Canada to control plant diseases caused by the Oomycetes or water-mould fungi. They inhibit protein (RNA) synthesis in fungi. The racemic mixture is registered for use as a seed treatment; the R-enantiomer is registered as a seed treatment as well as for field and greenhouse food and feed crops³, and nursery outdoor and greenhouse non-food crops (including conifers, ornamentals and turf). It is usually applied in the spring prior to planting/seeding, at 14-day intervals, for a total of up to 3 times on some crops and twice on others. The maximum application rate in Canada is 2.09 kg a.i./ha to the base of non-bearing apple trees. The end-use products are formulated as liquids, granules and ready-to-use liquids, and are applied using ground equipment, such as groundboom and low-pressure handwand.

³ Onion, lettuce, ginseng, potato, grape, potato, cucumber, strawberry, tobacco, hops, raspberry, snap beans, blueberry, apple, carrot

The American and Canadian use patterns were compared. The Canadian formulation types of end-use products and use sites are among those registered in the United States. The maximum application rate in Canada is 2.09 kg a.i./ha (applied to the base of non-bearing apple trees), which is lower than the maximum registered rate in the United States (i.e. 5.6 kg a.i./ha applied to conifers). The R-enantiomer is applied up to three times per growing season in Canada while, in the United States, it could be applied up to four times. The Canadian potential application methods are among those registered in the United States. Some use sites are unique to Canada⁴; however, in the United States, there are registered uses on golf course turf, in greenhouse and for seed treatment. Based on this comparison of use patterns and despite differences between Canada and the United States, it was concluded that the USEPA RED and Federal Register document for the racemic mixture and R-enantiomer are an adequate basis for the re-evaluation of the Canadian uses of the racemic mixture and R-enantiomer.

All current uses are being supported by the registrants and were, therefore, considered in the re-evaluation of the racemic mixture and R-enantiomer. Appendix II lists all metalaxyl racemic mixture and R-enantiomer products that are registered as of 4 July 2007, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 1994 RED on metalaxyl (the racemic mixture), the USEPA concluded that the end-use products formulated with the racemic mixture, registered at the time of the RED publication, would not pose unreasonable risks or adverse effects to humans or the environment; therefore, they were eligible for re-registration. After the RED, the USEPA published a Federal Register document in 2001 for the R-enantiomer (metalaxyl-M), which included an aggregate risk assessment meeting the safety standard under the American *Food Quality Protection Act* requirements. Based on bridging data showing structural similarity between the racemic mixture and R-enantiomer, the USEPA concluded that environmental fate, chemistry and toxicology data for the racemic mixture also applied to the R-enantiomer and could be used for the purposes of this aggregate risk assessment. Therefore, the environmental fate and toxicity described in the USEPA RED document was not revisited for the 2001 aggregate assessment.

Similarly, the PMRA also determined that the R-enantiomer was considered to be toxicologically equivalent to the racemic mixture and to have similar environmental fate characteristics. On this basis, the conclusions drawn in the USEPA RED document regarding the racemic mixture are considered to be an adequate basis for the re-evaluation of both forms of metalaxyl.

⁴ Sod farm, greenhouse cucumber, greenhouse tobacco seed bed, seed treatment of carrot, spinach, mustard, rapeseed and sainfoin.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to metalaxyl racemic mixture and R-enantiomer could occur by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required. The toxicological endpoints selected by the USEPA for assessment of risk from occupational exposure are summarized in Appendix III.

Workers can be exposed to metalaxyl racemic mixture and R-enantiomer through mixing, loading or applying the pesticide and when entering a treated site to conduct activities such as scouting and/or handling of treated crops.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

It was determined that there were several potential exposure scenarios for occupational handlers of metalaxyl racemic mixture and R-enantiomer. Specifically, exposure could occur during, for example, open mixing of liquids for foliar application to onions using centre pivot irrigation or loading of the granular formulation for soil broadcast treatment to non-bearing nut trees using groundboom equipment. However, it was also determined that there were no relevant endpoints of toxicological concern; therefore, a quantitative exposure and risk assessment was not conducted. A general label statement for basic hygiene was required for occupational, non-Worker Protection Standard (WPS) (non-agricultural) uses in the United States.

The USEPA RED adequately addressed potential exposure scenarios associated with the uses of the racemic mixture and R-enantiomer in Canada, with the exception of the use on sod farms. Exposure of the mixer/loader/applicator to the R-enantiomer may be greater from use on sod farms than on golf course turf, based on area treated per day (30 ha for sod farms versus 16 ha for golf course turf). In 2004, the PMRA conducted an occupational and postapplication risk assessment in which a MOE for the mixer/loader/ applicator on sod farms (MOE = 1243) was

found to be acceptable, based on combined risk from dermal and inhalation exposure. This assessment used the Pesticide Handlers Exposure Database (PHED) data, with an assumed application rate of 0.768 kg a.i./ha (the current label rate), and assuming personal protective equipment (PPE) of a long-sleeved shirt, long pants and gloves.

For all other uses, conclusions derived from the RED apply to the Canadian situation. Based on this, the PMRA requires instructions on labels concerning good hygiene practices. Based on a review of current labels, recommendations for PPE on Canadian labels were found to be adequate. However, for the purposes of basic hygiene, the label for the granular formulation used on carrot, lettuce and ginseng must be amended to include chemical-resistant gloves during mixing, loading, clean-up and repair. The proposed label amendments are listed in Appendix IV.

3.1.1.2 Postapplication Exposure and Risk

The USEPA did not assess occupational postapplication risks to agricultural workers because no relevant toxicological endpoints of concern were identified.

The 1992 USEPA Worker Protection Standard is intended to decrease the number of injuries from handling pest control products. A restricted-entry interval (REI) is the period of time following a pesticide application during which workers are not allowed to re-enter the treated area. According to the WPS, the length of the REI is determined by the toxicity of the active ingredient. In lieu of a postapplication risk assessment, an REI of 24 hours for all metalaxyl racemic mixture and R-enantiomer agricultural uses was required in the United States. In addition, general good hygiene label statements were required for occupational postapplication exposure for non-agricultural uses, such as professional application to industrial lawns (including golf courses), residential lawns and ornamental beds.

Exposure of workers in Canada performing postapplication activities on sod farms was not addressed specifically in the USEPA RED document, as this was not a registered use. In 2004, the PMRA conducted a postapplication occupational risk assessment for sod farm use, based on the potential for short-term exposure to workers re-entering sod farm turf that has been treated with the R-enantiomer. The PMRA concluded that risk was acceptable ($MOE = 123$) on day 0 after application. In addition, it is expected that some of the postapplication scenarios addressed in the USEPA RED document would represent higher potential exposure (e.g. foliar spray on grapes) than use on sod farms.

Use on greenhouse tobacco seedbeds and cucumber, as a soil drench, is not registered in the United States. However, it is not expected that postapplication exposure from these scenarios would be higher than exposure from other greenhouse scenarios addressed in the RED document (e.g. greenhouse ornamentals). It should also be noted that potential re-entry exposure from use on cucumber would be expected to be minimal, based on the label requirement that the product not be applied to the foliage, but only to the growing media at the base of each plant.

Despite some differences noted above in the use pattern between Canada and the United States, the PMRA considers that conclusions found in the RED document on postapplication exposure and risk are relevant to the Canadian scenario.

Currently registered uses of metalaxyl R-enantiomer in Canada include foliar spray (by ground or aerial application), soil drench applications to agricultural crops, application to turf (golf course or sod farm), and to seed. Current Canadian labels include a 12-hour REI for turf.

For products applied as a soil drench by ground application (Registration Number 25384 and 26612), a 12-h REI is considered to be adequate. This is based on the use pattern of the R-enantiomer (applied early in the season, to the soil), where the potential for contact with the active ingredient's residue is limited and on the general toxicological profile of metalaxyl as assessed in the RED (no trigger for a quantitative postapplication risk assessment).

For turf uses, previous PMRA risk assessments have shown acceptable risk at day 0 for use on sod farm. This is consistent with the results of the USEPA postapplication risk assessment for residential use on turf (see Section 3.1.2.1). Based on this, the current Canadian 12-hour REI for use on turf is considered to be adequate (Registration Number 27055).

For products applied to agricultural crops later in the season as a foliar spray (Registration Number 25379, 25419 and 26643), where postapplication contact with residues of the R-enantiomer is more likely, a 24-h REI, consistent with the metalaxyl RED recommendation, is required.

The requirement of an REI is not applicable to seed treatment. All labels of products currently registered for seed treatment include a requirement to wear a long-sleeved shirt, long pants and chemical-resistant gloves during mixing, loading and application, and a dust mask when bagging or sewing bags of treated seeds, with the exception of labels for two products containing the racemic mixture. For basic hygiene purposes and for label consistency, labels of the racemic mixture and R-enantiomer products registered for seed treatment in Canada must include the requirement of a dust mask when handling treated seed.

Most labels of products registered for seed treatment include a precautionary statement for bags of treated seed. The PMRA requires that this statement be on all labels of products registered for seed treatment.

Proposed label amendments are listed in Appendix IV.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach as explained for occupational exposure and risk assessment in Section 3.1.1. The toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix III.

In the United States, metalaxyl racemic mixture and R-enantiomer are registered for use on residential turf. Homeowners can be exposed to metalaxyl racemic mixture and R-enantiomer when mixing, loading or applying the pesticide and when re-entering a treated site. Toddlers can be exposed via "hand-to-mouth" and "object-to-mouth" activities and through incidental soil ingestion.

Short-term risk to adults from mixing/loading/application inhalation exposure as well as risk to toddlers from postapplication incidental oral exposure were assessed. Postapplication inhalation exposure was not considered to be a significant route of exposure. Dermal toxicity endpoints for short- or intermediate-term exposure were not identified. MOEs did not exceed the USEPA's level of concern.

There are no residential or homeowner uses currently registered in Canada. Potential exposure to golfers is discussed under the aggregate risk assessment, in Section 3.1.2.4.

3.1.2.2 Exposure From Food and Drinking Water

The USEPA did not identify an acute toxicological endpoint of concern. On this basis, an acute risk assessment was not conducted.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it is expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix III).

A Tier I chronic dietary risk assessment due to risk from food and drinking water was conducted using the Dietary Exposure Evaluation Model (DEEM), which incorporates food consumption data from the United States Department of Agriculture 1994–1996 Continuing Surveys of Food Intake by Individuals (CSFII). This resulted in estimated exposure from food of 36% of the cPAD for the most sensitive subpopulation, children 1–6 years old. This assessment was based on a cPAD of 0.074 mg a.i./kg bw/day, which was calculated from a 6-month feeding study in dogs (no observed adverse effect level [NOAEL] of 7.41 mg/kg bw/day and 100-fold uncertainty factor). It was assumed that 100% of crops were treated, and both established and proposed tolerance residue levels (the enforceable, maximum permissible level of an active ingredient on food) were used.

Exposure to pesticides through drinking water can occur as a result of groundwater or surface water contamination. Both acute (one day) and chronic (multiple year) drinking water risks are considered, using either modelling or actual monitoring data, if available, to estimate those risks. Modelling is carried out in tiers of increasing refinement, but is designed to provide high-end estimates of exposure. The risk assessment may be conducted by the drinking water level of comparison (DWLOC) approach or assessed probabilistically in DEEM/Lifeline.

For metalaxyl racemic mixture and R-enantiomer, drinking water exposure was addressed by calculating DWLOCs. In order to determine the maximum allowable contribution from water in the diet, it was first determined how much of the overall risk was contributed by food; following this, the DWLOC was determined. The DWLOC represents the maximum allowable contribution to the human diet that may be attributed to residues of a pesticide in drinking water after dietary exposure is subtracted from the aPAD or cPAD.

It was reported that metalaxyl racemic mixture was persistent, mobile, and would leach into groundwater in various soils. The USEPA concluded that registered uses of the racemic mixture would result in groundwater contamination. Based on sufficient bridging data for the racemic mixture, the environmental fate of the R-enantiomer was expected to be similar to that of the racemic mixture. Residues to be included in the drinking water assessment were the racemic mixture, the R-enantiomer and their metabolites containing the 2,6-dimethylaniline moiety, each expressed as parent equivalents. Therefore, the USEPA required the addition of a groundwater statement on product labels.

The USEPA reported that insufficient monitoring exposure data were submitted, and drinking water exposure and risk were assessed using Tier I modelling data generated by the Generic Estimated Environmental Concentration (GENEEC) model for surface water and the SCI-GROW model for groundwater. The model estimates were based on the maximum lingonberry application rate of 3.025 kg a.i./ha applied twice per year for a total of 6.05 kg a.i./ha/year. Combined expected environmental concentrations (EECs) for chronic exposure to surface water were estimated to be 101 ppb, and for groundwater to be 51 ppb, for all populations.

In Canada, metalaxyl racemic mixture and R-enantiomer are currently registered for seed treatment, and the R-enantiomer is registered for use on field and greenhouse food/feed and non-food/non-feed crops. Of these, three Canadian commodities were not included in the USEPA dietary risk assessment, i.e. seed treatment of mustard, rapeseed and sainfoin, because these are not registered uses in the United States. Despite this, the USEPA conclusions are considered to be relevant to the Canadian use pattern because the USEPA aggregate risk assessment is considered to be conservative as it was based on tolerance residue levels. Further, their Tier I estimates of exposure from food residues filled a relatively small portion of the risk cup, and seed treatment of mustard, rapeseed and sainfoin will likely result in minimal food residue because the treated seed is for planting only and not for food/feed. The American tolerances used in the risk assessment were equal to Canadian maximum residue limits (MRLs) (i.e. 0.1 ppm general MRL⁵)

Both metalaxyl racemic mixture and R-enantiomer are considered to be mobile and persistent by the USEPA; however, no water monitoring data were required as a result of the 1994 USEPA RED. The USEPA aggregate risk assessments published in a 2001 Federal Register showed

⁵ Changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

acceptable risk based on conservative parameters (conservative Tier I model estimates of water concentration based on an application rate of 3.025 kg a.i./ha, applied twice per year, which is higher than the maximum Canadian application rate of 2.09 kg a.i./ha, applied twice per year). Based on USEPA conclusions, the PMRA requires a label statement to mitigate groundwater contamination and does not require additional water monitoring data at this time.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to the racemic mixture and R-enantiomer (i.e. from food, water and residential exposures). Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures. Short-term and intermediate aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

An acute aggregate risk assessment was not performed because an acute reference dose (ARfD) was not identified.

It was determined that there was potential for short- and intermediate-term residential exposure. The USEPA short-term and intermediate aggregate risk assessments took into account residential exposure and chronic food and drinking water exposure (considered to be a background exposure level). For the American adult population, EECs of 51 ppb and 101 ppb (groundwater and surface water, respectively) were below the adult short-term DWLOC of 17 000 ppb and below the adult intermediate-term DWLOC of 2100 ppb. For toddlers, these EECs were below the toddler short-term DWLOC of 4600 ppb and were also below the toddler intermediate-term DWLOC of 420 ppb.

The USEPA's chronic aggregate risk assessment was based on exposure to food and drinking water. For toddlers, the most sensitive subpopulation, these EECs were below the toddler chronic DWLOC of 460 ppb.

Based on these assessments, the USEPA concluded with reasonable certainty that no harm would result for the general population as well as for infants and children from aggregate exposure to residues of metalaxyl racemic mixture and R-enantiomer.

In Canada, metalaxyl racemic mixture and R-enantiomer are currently registered for seed treatment, and the R-enantiomer is registered for use on field and greenhouse food/feed and non-food/non-feed crops. There are no residential or homeowner uses currently registered in Canada, but there is potential for exposure to golfers. Due to these uses and based on the environmental fate of the R-enantiomer, there is a potential for contamination of groundwater and surface water.

Three Canadian commodities were not included in the USEPA dietary risk assessment reported in the Federal Register document because these are not registered American uses. These were seed treatment of mustard, rapeseed and sainfoin. Despite this, the USEPA conclusions are

considered to be relevant to the Canadian use pattern because the USEPA aggregate risk assessment was considered to be conservative, based on the following:

- tolerance residue levels;
- Tier I drinking water modelling - the maximum Canadian application rate is 2.09 kg a.i./ha, applied twice per year, which is lower than that assumed in the USEPA drinking water assessment;
- the USEPA aggregate risk assessment included exposure in residential settings on turf (which should address Canadian turf use on golf courses); and
- seed treatment of mustard, rapeseed and sainfoin is for seed to be planted and likely to result in minimal food residue.

3.1.3 Cumulative Effects

The USEPA has not determined whether metalaxyl racemic mixture and R-enantiomer have a common mechanism of toxicity with other substances or whether they share a toxic metabolite produced by other substances. Therefore, it was assumed that the racemic mixture and R-enantiomer do not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

Metalaxyl racemic mixture was found to be persistent and mobile in the environment. Therefore, it was found to have the potential to reach surface water via runoff and/or spray drift and to contaminate groundwater via leaching. It was shown in terrestrial studies to dissipate by aerobic soil metabolism, by plant uptake, and by leaching into groundwater. Monitoring studies demonstrated that the racemic mixture and its primary degradate, CGA-62826, had the potential to reach groundwater and surface water. In addition, results from other groundwater and drinking water monitoring studies (site not specified), although inadequate for use in USEPA assessments, showed that the racemic mixture had the potential to reach groundwater, where levels of the racemic mixture had been detected at up to 3 ppb. It was concluded that registered uses of the racemic mixture would result in contamination of groundwater; therefore, the addition of a groundwater statement on product labels was required.

To assess the ecological risk of the racemic mixture to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs).

Risk assessments for terrestrial insects and mammals were not performed because the racemic mixture was found to be practically non-toxic to these groups of organisms. As a result, the potential for the racemic mixture to have adverse effects on terrestrial insects, mammals and plants was expected to be low. Terrestrial plant exposure and risk were not addressed.

For terrestrial animal exposure and risk assessment for acute risks from non-granular formulations, the USEPA predicted the maximum expected terrestrial residues (i.e. EECs) based on a single application at different application rates (up to 9 kg a.i./ha) and on different categories of avian food items. For granular formulations, acute risks to birds were analyzed by measuring the LD₅₀/square foot. Based on a result of 0.039 LD₅₀/square foot (LOC was 0.5 LD₅₀/square foot), it was concluded that the acute risk from granular formulations to exposed birds was minimal. A similar conclusion was reached regarding non-granular formulations (RQ of 0.038; LOC of 0.5). No chronic avian data were available, and due to metalaxyl racemic mixture's widespread use in the United States (registered on more than 100 agricultural crops), multiple applications as well as persistence in the field, the USEPA required confirmatory avian reproductive toxicity studies in order to assess the risk to avian species from chronic exposure to the racemic mixture.

For aquatic exposure and risk assessment, EECs were calculated based on different application rates (up to 9 kg a.i./ha) for the following:

- ground application, on a 10-acre field treated by unincorporated ground application and draining into a 6-foot-deep, 1-acre water body;
- aerial application, total loading from both runoff (1%) and drift (5%) of a 10-acre field and draining into a 6-foot-deep, 1-acre water body;
- single, inadvertent direct application to a 6-foot-deep, 1-acre water body.

For freshwater and estuarine fish and invertebrates, RQs based on acute exposure ranged from 0.0004 to 0.012, below the LOC of 0.5. The chronic RQ of 0.023 was below the LOC of 1.0. For aquatic plants, the RQ of 0.00038 was below the LOC of 1.0.

Based on the RQs, the USEPA concluded that the racemic mixture posed minimal, if any, risk to terrestrial and aquatic non-target organisms, including birds, small mammals, fish, estuarine species, honeybees and aquatic plants. The registered uses of the racemic mixture did not present an acute hazard to endangered terrestrial and aquatic animals nor to endangered aquatic plant species. Chronic risks to birds could not be assessed, and confirmatory avian reproduction studies were required.

Although no levels of concern were exceeded, the USEPA required an environmental hazard label statement to minimize exposure of non-target species from direct application, spray drift and/or runoff from treated areas.

Conclusions drawn in the 1994 USEPA RED regarding environmental fate and ecological risks for the racemic mixture also apply to the R-enantiomer. The racemic mixture is only registered for seed treatment in Canada. The maximum registered terrestrial application rate of the R-enantiomer in Canada is 2.1 kg a.i./ha, which corresponds to a rate of 4.2 kg a.i./ha of the racemic mixture; this rate is encompassed by the rates used in the USEPA ecological risk assessments.

Based on the USEPA RED document and the Canadian use pattern, the PMRA will require that a groundwater label advisory statement be on all end-use product labels. The PMRA also requires, on all product labels, standard statements concerning runoff. These proposed label amendments are listed in Appendix IV.

The PMRA has reviewed the environmental toxicology and fate data for metalaxyl R-enantiomer, as provided in the 1994 USEPA RED document, and determined that buffer zones are not required for the protection of sensitive aquatic habitats. However, the PMRA could not determine the risk posed by the R-enantiomer to sensitive terrestrial habitats due to a lack of terrestrial vascular plant toxicity data. Risks to terrestrial plants cannot be assessed based on effects seen in aquatic vegetation. Therefore, the PMRA will require data in order to calculate terrestrial buffer zones. Proposed label amendments are listed in Appendix IV. Inputs to buffer zone models are described in Appendix V.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track-1 substances.

The federal Toxic Substances Management Policy and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of metalaxyl racemic mixture and R-enantiomer. The PMRA has reached the following conclusions.

- The racemic mixture and R-enantiomer are not bioaccumulative, the bioconcentration factor for the racemic mixture was ≤ 7 times for the whole fish, which is well below the TSMP threshold value of 5000 times. In addition, the *n*-octanol—water partition coefficient ($\log K_{ow}$) of the racemic mixture is 1.75 at pH 7, and that of the R-enantiomer is 1.71 at pH 7, which are below the TSMP threshold value of 5. The racemic mixture and R-enantiomer do not meet all TSMP Track-1 criteria; thus, they are not candidates for Track-1 classification.
- Based on a review of the available chemistry information (see Section 2.1), the technical products are not expected to contain impurities of toxicological concern as identified in Regulatory Directive DIR98-04 or TSMP Track-1 substances as identified in Appendix II of Regulatory Directive DIR99-03.

- Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*, published on 31 May 2006.

4.0 OECD Status of Metalaxyl and Metalaxyl-M

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the currently available information on the status of metalaxyl in other OECD member countries, metalaxyl was not approved for inclusion in the list of active ingredients authorized for use as plant protection products in the European Union (i.e. Annex I to Directive 91/414/EEC) because the manufacturer chose not to participate in the review programme and did not submit the data necessary to complete the review (EC, 2003).

As described earlier in this document, the United States, also an OECD member, assessed the registration of all uses of all metalaxyl and metalaxyl-M uses in 1994 and 2001, and concluded that uses of metalaxyl and metalaxyl-M as pesticides do not result in unreasonable adverse effects to human health or the environment provided the risk-reduction measures recommended in the RED document and Federal Register document are implemented.

In addition, the Canadian re-evaluation of metalaxyl is largely based on the 1994 USEPA assessments and on an aggregate risk assessment conducted by the USEPA in 2001. As described in this document, the PMRA has found the USEPA human health and environmental risk conclusions to be relevant to the Canadian uses of metalaxyl and metalaxyl-M. Measures to protect workers are required, including personal protective equipment and restricted-entry intervals. To mitigate potential contamination of water and non-target terrestrial habitats, additional environmental hazard label statements are required. In addition, non-target plant data are required to calculate terrestrial buffer zones.

Therefore, all aspects regarding effects to human health or the environment from currently registered uses of the active ingredients metalaxyl and metalaxyl-M were taken into consideration in their re-evaluation in Canada and have been addressed in the proposed Canadian re-evaluation decision.

5.0 Proposed Re-evaluation Decision

The PMRA has determined that metalaxyl (racemic mixture) and metalaxyl-M (the R-enantiomer) are acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. Canadian end-use product labels must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrants of the technical active ingredient products are required to submit data as a condition of continued registration under Section 12 of the *Pest Control Products Act*. Appendix I lists the data requirements.

6.0 Data Required as Condition of Continued Registration

In order for the PMRA to complete terrestrial buffer zone calculations, the following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of the racemic mixture and R-enantiomer must provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that the PMRA will send to registrants of the technical grade active ingredient.

- These following studies must be conducted according to the appropriate Office of Prevention, Pesticides and Toxic Substances (OPPTS) guidelines indicated.
- DACO 9.8.4: Terrestrial Vascular Plants—Seedling Emergence (USEPA OPPTS 850.4100 guideline) and Vegetative Vigour (USEPA OPPTS 850.4150 guideline).

Should the registrants fail to submit these studies within the specified timeline, conservative buffer zones for the protection of sensitive terrestrial habitats will be required on product labels.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for metalaxyl is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm. (accessed 22 July 2007).

The USEPA Federal Register environmental document (Mefenoxam; Pesticide Tolerance. Federal Register, 17 September 2001) is available on the USEPA website at www.epa.gov/fedrgstr/EPA-PEST/2001/September/Dav-17/p23088.htm (accessed 22 July 2007).

The European Commission document (2003/308/EC), *Commission Decision of 2 May 2003 concerning the non-inclusion of metalaxyl in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant-protection products containing this active substance*, is available on the Official Journal of the European Union website at [http://eur-lex.europa.eu/JOHtml.do?uri=OJ:L:2003:113:SOM: EN:HTML](http://eur-lex.europa.eu/JOHtml.do?uri=OJ:L:2003:113:SOM:EN:HTML) (accessed 22 July 2007).

List of Abbreviations

λ	lambda
a.i.	active ingredient
aPAD	acute population adjusted dose
ARfD	acute reference dose
CAS	Chemical Abstracts Service
cPAD	chronic population adjusted dose
CSFII	Continuing Survey of Food Intakes by Individuals
DACO	data code
DEEM	Dietary Exposure Evaluation Model
DT ₅₀	dissipation time to 50%
DWLOC	drinking water level of concern
EEC	expected environmental concentration
FQPA	<i>Food Quality Protection Act</i>
g	gram
GENEEC	Generic Estimated Environmental Concentration
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K _{ow}	<i>n</i> -octanol—water partition coefficient
L	litre
LC ₅₀	median lethal concentration
LOC	level of concern
m	metre
m ³	metre(s) cubed
mg	milligram
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
OPPTS	Office of Prevention, Pesticides and Toxic Substances
pH	-log 10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
pKa	-log 10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
REI	restricted-entry interval
RfD	reference dose
RVD	Re-evaluation Decision
RQ	risk quotient

SCI-GROW	Screening Concentration In Ground Water (model)
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
WPS	Worker Protection Standard

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of the racemic mixture and R-enantiomer are required to provide these data within the timeline specified in the decision letter the PMRA will send.

- DACO 9.8.4: Terrestrial Vascular Plants - Seedling Emergence (USEPA OPPTS 850.4100 guideline) and Vegetative Vigour (USEPA OPPTS 850.4150 guideline)]. These studies must be conducted according to the appropriate OPPTS guidelines indicated.

Should the registrants fail to submit these studies within the specified timeline, conservative buffer zones for the protection of sensitive terrestrial and aquatic habitats will be required on product labels.

Appendix II Products Containing Metalaxyl and Metalaxyl-M and Registered in Canada as of 4 July 2007

Reg. No.	Marketing Class	Registrant	Product Name	Guarantee (% a.i.)	Formulation Type
METALAXYL PRODUCTS					
26644	Technical	Bayer CropScience Inc.	Gustafson Metalaxyl Technical	97	Dust
24262	Commercial	Bayer CropScience Inc.	Apron FL Seed Treatment	317 g/L (= 28.1%)	Suspension
26674	Commercial	Bayer CropScience Inc.	Allegiance FL Seed Treatment	317 g/L (= 28.1%)	Suspension
27564	Commercial	Bayer CropScience Inc.	Prosper FL Insecticide and Fungicide Seed Treatment	4 g/L (= 0.04%)	Suspension
27692	Commercial	Bayer CropScience Inc.	Raxil MD Fungicide	6.6 g/L (= 0.06%)	Suspension
METALAXYL-M PRODUCTS					
25372	Technical	Syngenta Crop Protection Canada Inc.	Metalaxyl-M Technical	97%	Liquid
25379	Commercial	Syngenta Crop Protection Canada Inc.	Ridomil Gold MZ 68WP	4%	Wettable powder
25384	Commercial	Syngenta Crop Protection Canada Inc.	Ridomil Gold 480EC	480 g/L (= 42.6%)	Emulsifiable concentrate
25419	Commercial	Syngenta Crop Protection Canada Inc.	Ridomil Gold MZ 68WP Water Soluble Bag	4%	Wettable powder
25585	Commercial	Syngenta Crop Protection Canada Inc.	Apron XL LS	33.3%	Suspension
25777	Commercial	Syngenta Crop Protection Canada Inc.	Dividend XL RTA Fungicide	0.27%	Suspension
25778	Commercial	Syngenta Crop Protection Canada Inc.	Dividend XL	1.38%	Suspension
26443	Commercial	Syngenta Crop Protection Canada Inc.	Ridomil Gold/Bravo Twin-Pak	480 g/L (= 42.6%)	Suspension
26612	Commercial	Syngenta Crop Protection Canada Inc.	Ridomil Gold 1G	1%	Granule
26637	Commercial	Syngenta Crop Protection Canada Inc.	Helix Liquid Seed Treatment	0.39%	Solution
26638	Commercial	Syngenta Crop Protection Canada Inc.	Helix Xtra Seed Treatment	0.39%	Solution

Reg. No.	Marketing Class	Registrant	Product Name	Guarantee (% a.i.)	Formulation Type
27055	Commercial	Syngenta Crop Protection Canada Inc.	Subdue MAXX	240 g/L (= 21.3%)	Emulsifiable concentrate
27071	Commercial	Syngenta Crop Protection Canada Inc.	Maxim XL Seed Treatment Fungicide	8.4%	Solution
27307	Commercial	Syngenta Crop Protection Canada Inc.	Helix Xtra Colourless Seed Treatment	0.39%	Solution
27312	Commercial	Syngenta Crop Protection Canada Inc.	Helix Colourless Seed Treatment	0.39%	Solution
27577	Commercial	Syngenta Crop Protection Canada Inc.	Apron MAXX RTA	1.10%	Ready-to-use liquid
27650	Commercial	Syngenta Crop Protection Canada Inc.	Tribune Seed Treatment Fungicide	0.51%	Ready-to-use liquid
28474	Commercial	Syngenta Crop Protection Canada Inc.	Ridomil Gold 480SL Fungicide	480 g/L (= 42.6%)	Solution

Appendix III Toxicological Endpoints Selected by the USEPA for the Metalaxyl and Metalaxyl-M Health Risk Assessments

Exposure Scenario (route and period of exposure)	Dose (mg/kg bw/day)	Study	Endpoint and UF/FQPA SF ^{a,b}
Dietary chronic	Oral NOAEL = 7.41	Six-month feeding study in dogs	UF = 100-fold cRfD = 0.074 mg/kg bw/day FQPA SF = 1-fold cPAD = 0.074 mg/kg bw/day
Dermal long-term residential	Oral NOAEL = 7.41	Six-month feeding study in dogs	UF = 100-fold FQPA SF = 1-fold Target MOE = 100
Inhalation short-term residential	Oral NOAEL = 50	Developmental tox study in rats	UF = 100-fold FQPA SF = 1-fold Target MOE = 100
Inhalation intermediate residential	Oral NOAEL = 7.41	Six-month feeding study in dogs	UF = 100-fold FQPA SF = 1-fold Target MOE = 100
Inhalation long-term residential	Oral NOAEL = 7.41	Six-month feeding study in dogs	UF = 100-fold FQPA SF = 1-fold Target MOE = 100
Incidental oral short-term residential	Oral maternal NOAEL = 50	Developmental tox study in rats	UF = 100-fold FQPA SF = 1-fold Target MOE = 100
Incidental oral intermediate	Oral NOAEL = 7.41	Six-month feeding study in dogs	UF = 100-fold FQPA SF = 1-fold Target MOE = 100

^a FQPA SF = *Food Quality Protection Act* safety factor; target MOE = desired margin of exposure for occupational or residential assessments.

^b FQPA SF set at 1-fold because (1) there was no indication of quantitative or qualitative increased susceptibility of rats or rabbits to in utero and/or postnatal exposure, (2) a developmental neurotoxicity study was not required, and (3) the dietary (food and drinking water) and non-dietary exposure assessments would not underestimate the potential exposures for infants and children.

Appendix IV Label Amendments for Products Containing Metalaxyl (racemic mixture) and Metalaxyl-M (R-enantiomer)

The labels of racemic mixture and R-enantiomer end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

The following statements must be included in the section entitled **DIRECTIONS FOR USE**.

Do not apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands), estuaries or marine habitats.

Do not contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

The following statements must be included in the section entitled **DIRECTIONS FOR USE** for products used on field crops, except those having a granular formulation.

- for airblast application:

Do not apply during periods of dead calm. Avoid application of this product when winds are gusty. Do not direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. Do not apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

- for aerial application:

Do not apply during periods of dead calm. Avoid application of this product when winds are gusty. Do not apply when wind speed is greater than 16 km/h at flying height at the site of application. Do not apply with spray droplets smaller than the American Society of Agricultural and Biological Engineers medium classification.

- for field sprayer application:

Do not apply during periods of dead calm. Avoid application of this product when winds are gusty. Do not apply with spray droplets smaller than the American Society of Agricultural and Biological Engineers classification.

- for all labels with field applications:

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

The following statements must be included in the section entitled **PRECAUTIONS**.

- for all end-use products:

Do not apply in a way that this product will contact workers or other persons, either directly or through drift. Only handlers (mixers, loaders and applicators) wearing personal protective equipment may be in the area being treated during application.

- for products having seed treatment uses:

Wear a suitable dust mask when bagging or sewing bags of treated seed or when transferring seed to a storage bin.

All bags containing treated seed for sale or use in Canada must be labelled or tagged as follows: "This seed has been treated with [product name] fungicide containing [metalaxyl or metalaxyl-M]. Use chemical-resistant gloves when handling treated seed.

- for all products having foliar application (conifers, ornamentals, grape, ginseng, lettuce, onion and potato):

Do not enter or allow worker entry into treated areas for 24 hours following application.

- for all products having soil drench application:

Do not enter or allow worker entry into treated areas for 12 hours following application.

- for all products having food and/or feed uses:

If this pest control product is to be used on a commodity that may be exported to the United States and you require information on acceptable residue levels in the United States, contact 1-866-375-4648 or www.croplife.ca.

The following statements must be included in the section entitled In the **ENVIRONMENTAL HAZARDS**.

The use of this product may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow.

To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. compacted or fine-textured soils such as clay).

Avoid application of this product when heavy rain is forecast.

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements. Based on basic hygiene and for label consistency, chemical-resistant gloves must be added to the list of PPE for mixing, loading, application, clean-up and repair activities for end-use products having the granular formulation and applied by groundboom equipment.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

Appendix V Inputs to Buffer Zone Models for Metalaxyl-M

Ground Use Data (from Canadian labels)				
Crop	Formulation Type	Method of Application	Number of Application	Maximum Application Rate (g a.i./ha)
Ornamentals	Emulsifiable concentrate	Ground	1	500
Tobacco	Emulsifiable concentrate	Ground	1	576
Turf	Emulsifiable concentrate	Ground	1	770
Grape	Wettable powder	Early airblast	1	120
Grape	Wettable powder	Late airblast	1	120

Model Input Data for Aquatic Buffer Zones (from 1994 RED)		
Half-life for aquatic buffer zones	N/A	Assumed stable
Most sensitive freshwater species	<i>Daphnia magna</i>	NOEC = 1.27 mg a.i./L; effect not specified, lifecycle test
Most sensitive estuarine/marine species	<i>Crassostrea virginica</i>	LC ₅₀ = 4.4 ppm ∴ NOEC = 0.44 mg a.i./L; effect not specified

Model Input Data for Terrestrial Buffer Zones (from 1994 RED)		
Half-life for terrestrial buffer zones	Aerobic soil DT ₅₀	40 days
Most sensitive terrestrial plant species EC ₂₅ for vegetative vigour	<i>Lemna gibba</i>	EC ₂₅ for vegetative vigour was not available. EC ₅₀ = 92 ppm (terrestrial endpoint not available)

